

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of ) Group Art Unit: 1743  
Russell G. Higuchi )  
Serial No.: 08/968,208 )  
Filed: November 12, 1997 )  
For: **HOMOGENEOUS METHODS FOR** )  
**NUCLEIC ACID AMPLIFICATION** )  
**AND DETECTION** )

**For hand delivery to Examiner  
J. Snay in Group 1743 at 703-  
308-4032 on or after July 20,  
2001**

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Applicants submit herewith patents, publications or other information (listed on the attached Form 1449) for the Examiner's consideration. This Information Disclosure Statement, as far as is known to the undersigned, is being filed before the mailing date of a first Office action after the filing of a request for continued examination under § 1.114. A copy of each item listed on the Form 1449 is supplied herewith.

The present application is a division of application Ser. No. 07/695,201 filed May 2, 1991, now Patent No. 5,994,056, and is also related to Ser. No. 08/470,532 filed June 21, 1995, now Patent No. 6,171,785 (which is a continuation of Ser. No. 07/695,201), and to copending Ser. No. 08/266,061 filed July 5, 1994 (which is a continuation-in-part of Ser. No. 07/695,201). The granted patents are listed on the enclosed Form 1449, and copies are provided.

The Examiner's attention is also drawn to reference 19, which was made of record during prosecution of Patent No. 6,171,785. Limited information regarding this reference was provided in an Information Disclosure Statement submitted on November 14, 1994 during prosecution of

Ser. No. 08/266,061 (copy enclosed). Accordingly, no publication date is listed on the enclosed Form 1449 for this reference.

Reference 20 on the enclosed Form 1449 appears to correspond to the Gunther thesis citation that appears on page 65 of reference 19. A copy of the original German language document and an English translation are provided. According to information obtained by a German associate, reference 20 was deposited in the Library of the Max-Planck-Institute on July 20, 1999 and was added to the Library catalogue on August 2, 1999. As of May, 2001, this reference had not been deposited in any form in the Library of the University of Gottingen.

This Information Disclosure Statement is not intended to constitute an admission that any of the cited references is prior art. In accordance with 37 CFR §1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR §1.56(a) exists. The Examiner is respectfully requested to consider the listed references.

Respectfully submitted,

Date: July 19, 2001

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PATENT  
Atty. Docket No. 8977

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS : Russell G. Higuchi *et al.*  
SERIAL NO. : 08/266,061 GROUP ART UNIT: to be assigned  
FILED : July 5, 1994 EXAMINER: to be assigned  
DOCKET NO. : 8977  
TITLE : APPARATUS AND METHOD FOR MONITORING MULTIPLE AMPLIFICATION REACTIONS SIMULTANEOUSLY AND ANALYZING SAME

INFORMATION DISCLOSURE STATEMENT  
UNDER 37 C.F.R. §1.56, §1.97, AND §1.98

Hon. Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

The Examiner may find the following references and information, submitted in accordance with the duty of the disclosure under 37 C.F.R. §1.56, §1.97, and §1.98, material in the examination of the above-identified application. Copies of the references listed below and on the attached P.T.O. 1449 form are provided. The Examiner is requested to make these references of official record in the application.

The present invention is directed to a nucleic acid amplification detection method and apparatus that avoids the problems and disadvantages of the prior art. This goal is accomplished by providing an apparatus that monitors the amplification of multiple amplification reaction mixtures, simultaneously in real-time. In one embodiment, a CCD-camera detects the accumulation of double-stranded DNA (dsDNA) in each of multiple polymerase chain reactions simultaneously, using the increase in the fluorescence of a detectable fluorescent dye initially introduced into each amplification reaction mixture. The fluorescence results from the fluorescent dye binding duplex DNA. This embodiment advantageously eliminates the need for fiber-optic leads and the accompanying problems associated with coupling the fiber-optics to the individual reaction mixtures.

1. Bauer *et al.*, October, 1989, Proc. Natl. Acad. Sci. 86:7937-7941
2. Eigen, "Report on Evolution Research," Department of Biochemical Kinetics

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this 12 day of July, 1994.  
Rv

3. Higuchi *et al.*, April, 1992, Bio/Technology 10:413-417
4. Henco *et al.*, 1993, Chemical Abstracts 119:153368b
5. Higuchi *et al.*, September, 1993, Bio/Technology 11:1026-1030
6. U.S. Patent No. 4,856,073
7. U.S. Patent No. 5,038,852
8. U.S. Patent No. 5,049,490
9. U.S. Patent No. 5,210,015
10. European Patent Publication No. 266,881
11. European Patent Publication No. 487,218
12. European Patent Publication No. 512,334
13. PCT Patent Publication No. WO 92/05278
14. Japanese Patent Publication No. JP 3259099 (abstract)
15. Japanese Patent Publication No. JP 4027399 (abstract)
16. Japanese Patent Publication No. JP 4084751 (abstract)

Applicants note that they are not aware if the Eigen Report (Reference No. 2) has ever been published. Consequently, a publication date for this reference is not provided on the attached form. Although the preface of the Report has December 20, 1990, printed thereon, this may merely represent that the Report was completed by that date, but not necessarily published. However, pages i, 1, 2, 53-56, and 65 of the Report, as well as the title page, became available to Applicants more than one year before the filing of this application. Accordingly, these pages are enclosed with this statement.

This Information Disclosure Statement under 37 C.F.R. §1.56, §1.97, and §1.98 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that this citation constitutes prior art under 35 U.S.C. §102 and §103.

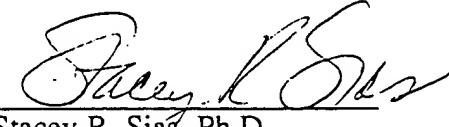
Since the Information Disclosure Statement is submitted before the mailing of the first Office Action on the merits, no fee is due.

PATENT  
Atty. Docket No. 8977

The Commissioner is hereby authorized to charge any fees in connection with this  
Information Disclosure Statement to Deposit Account No. 08-2525.

Respectfully submitted,

By:

  
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Stacey R. Sias, Ph.D.  
Agent for Applicants  
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November 14, 1994

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